REMARKS

Interview request

Applicants respectfully request a telephonic interview after the Examiner has reviewed the instant response and amendment. Applicants request the Examiner call Applicants' representative at (858) 720-5133.

Status of the Claims

Pending claims

Claims 1 to 30, 33 to 64, 66 to 71 and 83 to 98 will be pending and under consideration.

Claims added in the instant amendment

Claim 99 is added. Thus, after entry of the instant amendment, claims 1 to 30, 33 to 64, 66 to 71 and 83 to 99, will be pending and under consideration.

Outstanding Rejections

Claims 1 to 30, 33 to 64, 66 to 71 and 83 to 98 stand rejected under 35 U.S.C. §112, first paragraph, written description requirement. Applicants respectfully traverse all outstanding objections to the specification and rejection of the claims.

Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the new and amended claims. For example, support for claims encompassing the binding of cell surface receptor binding molecules to the cell surface receptor that do not induce apoptosis of the cell can be found, inter alia, in paragraph [0018] of U.S. Patent application publication no. 20040062756 ("the '756 publication"). support for claims encompassing the binding of cell surface receptor binding molecules to the cell surface receptor that result in cells being more receptive to transduction by a lentiviral vector can be found, inter alia, in paragraph [0017] and [0018] of the '756 publication.

Accordingly, no new matter has been added and the amendment can be properly entered.

Group and Species Restriction Requirement and Election

Applicants thanks the Office for reconsidering and withdrawing the restriction requirement; Claims 1 to 30, 33 to 64, 66 to 71 and 83 to 98 will be pending and under consideration.

Rejection Under 35 U.S.C. § 112, First Paragraph, Written Description

Claims 1 to 30, 33 to 64, 66 to 71 and 83 to 98 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. In particular, it is alleged, inter alia, that the specification fails to describe a representative number of species of the genera of (1) cell surface binding molecules, or (2) cell types, as discussed on pages 2 to 5, of the OA.

Cell surface binding molecules

The Office alleged that the term "cell surface binding molecule" fails to provide any meaningful structural limitations, for example, the molecule could comprise as few as two atoms or encompass, inter alia, any type of organic compound, nucleic acid, lipid and the like (see, e.g., page 4, lines 20 to 30, of the OA).

To address the Office's concerns, the claims have been amended to be directed to only one embodiment of the invention – where the cell surface binding molecule is a cell surface receptor binding molecule (in particular, independent claims 1 and 88 have been so amended; the third of the three pending independent claims, claim 34, already was limited to "contacting the [cells] ... with a lentiviral vector and an at least one molecule that physically interacts with a receptor, marker, or other recognizable moiety on the surface of the [cells]").

To further address the Office's concerns, all three pending independent claims have been amended to encompass only cell surface receptor molecules that do not induce apoptosis upon binding to the cell surface receptor. All three pending independent claims also have been amended to encompass only embodiments wherein the cell surface receptor binding molecule results in the cell being more receptive to transduction by the viral vector.

Applicants emphasize that the invention is not limited by any particular mechanism of action, as explained in paragraph [0017] of the '756 publication:

> [0017] The at least one molecule that binds the surface of the cells to be transduced includes any molecule that physically interacts with a receptor, marker, or other recognizable moiety on the surface of the cells. In principle, any cell surface binding molecule may be used for high efficiency transduction of cells. Without binding the invention to theory, the cell surface binding molecules may result in the host cell's chromatin being more receptive to DNA integration; in preferential integration of a viral vector into a site favorable for vector gene expression; in more efficient entry of the nucleic acid containing capsid into the cytoplasm; in more efficient entry of the virus across the cell membrane or internal membranous structures such as the endosome; or in making the cell more permissive for nuclear import of the viral vector's genetic material. The methods of the invention may also involve more than one of the above possibilities. Also, and as evident from the number and diversity of the above possibilities, the invention cannot be limited to any one theory. Instead, and given the extraordinary discovery of the invention in the stable transduction of up to 100% of the treated cells without negatively affecting the possible use of the cells in human therapy, the invention should be viewed as opening a new approach in the field of human cell therapy. [emphasis added]

Applicants also note that the specification expressly discloses many exemplary (alternative) cell surface receptor binding molecules, for example, an FLT-3 ligand; a TPO ligand Kit ligand; antibodies that have the same cell surface binding specificity as FLT-3, TPO, or Kit ligand; CD3 ligand; a CD28 ligand; a CD25 ligand; a CD71 ligand; a CD69 ligand; antibodies that have are the same cell surface binding specificity of CD3, CD25, CD28, CD69 or CD71 ligand (see, e.g., claim 19), or CD34, CD3, CD28, GM-CSF, IL-4, TNF-alpha; GM-CSF, interferon-alpha; antibodies or other binding molecules that have the same cell surface binding specificity as CD34, CD3, CD28, GM-CSF, IL-4, and TNF-alpha; GM-CSF or interferon-alpha (see, e.g., claim 22).

Cell Types

The Office alleged that the claims are directed toward an "inordinate number of cell targets" (see, e.g., page 5, lines 1 to 14, of the OA). To address the Office's concerns, as discussed above, the claims have been amended to be directed to only one embodiment of the invention – where the cell surface binding molecule is a cell surface receptor binding molecule. Thus, the claimed methods no longer encompass targeting an "inordinate number of cell targets".

Regarding the types of cells used to practice the claimed methods, Applicants respectfully note that independent claims 1 and 34 are focused on transducing only primary cells of the hematopoietic system and/or hematopoietic stem cells. Claim 88 is amended to be directed to transducing only primary cells of the hematopoietic system and/or hematopoietic stem cells (wherein the lentiviral vector is pseudotyped for targeting to a specific, desired cell type).

Applicants also note that the specification expressly discloses many exemplary (alternative) primary cells of the hematopoietic system and/or hematopoietic stem cells used to practice the

methods of the invention, including inter alia CD4 positive cells, lymphocytes or precursors thereof, CD8 positive cells, CD34 positive cells or precursors thereof.

In light of the instant amendment to the claims, and considering the many specific examples of exemplary (alternative) cell surface receptor binding molecules that can be used to practice the invention, and the many specific examples of exemplary (alternative) cell types that can be used to practice the claimed methods, Applicants respectfully aver that the specification reasonably conveyed to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

CONCLUSION

Applicants respectfully submit that after entry of the instant amendment all claims pending in this application are in condition for allowance. Applicants respectfully request withdrawal of the rejection under section 112, first paragraph. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

In the unlikely event that the transmittal form is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing 397272000401. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

As noted above, Applicants have requested a telephone conference with the undersigned representative to expedite prosecution of this application. After the Examiner has reviewed the instant response and amendment, please telephone the undersigned at (858) 720-5133.

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Respectfully submitted,

By _____

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